

WHAT IS CLAIMED IS:

1 1. A composition for delivery of a 5-HT agonist across the oral mucosa,
2 said composition comprising:

3 (a) a 5-HT agonist or a pharmaceutically acceptable salt thereof;

4 (b) a carrier; and

5 (c) a ternary buffer system comprising a carbonate salt, a bicarbonate salt, and a
6 metal oxide,

7 wherein said ternary buffer system raises the pH of saliva to a pH greater than about 9.9
8 irrespective of the starting pH of saliva.

1 2. A composition of claim 1, wherein said ternary buffer system raises the
2 pH of saliva to a pH of from about 9.9 to about 11 irrespective of the starting pH of saliva.

1 3. A composition of claim 1, wherein said 5-HT agonist is selected from
2 the group consisting of sumatriptan, naratriptan, rizatriptan, eletriptan, almotriptan,
3 zolmitriptan, frovatriptan, and combinations thereof.

1 4. A composition of claim 1, wherein said carbonate salt is selected from
2 the group consisting of sodium carbonate and potassium carbonate.

1 5. A composition of claim 1, wherein said bicarbonate salt is selected
2 from the group consisting of sodium bicarbonate and potassium bicarbonate.

1 6. A composition of claim 1, wherein said metal oxide is selected from
2 the group consisting of magnesium oxide and aluminum oxide.

1 7. A composition of claim 6, wherein said magnesium oxide is
2 amorphous magnesium oxide.

1 8. A composition of claim 1, wherein said ternary buffer system
2 comprises sodium carbonate, sodium bicarbonate, and amorphous magnesium oxide.

1 9. A composition of claim 1, wherein said carrier is selected from the
2 group consisting of a binder, a gum base, and combinations thereof.

1 10. A composition of claim 9, wherein said gum base comprises at least
2 one hydrophobic polymer and at least one hydrophilic polymer.

- 1 **11.** A composition of claim 9, wherein said binder is selected from the
2 group consisting of a sugar, a sugar alcohol, and combinations thereof.
- 1 **12.** A composition of claim 11, wherein said sugar alcohol is selected from
2 the group consisting of mannitol, sorbitol, xylitol, and combinations thereof.
- 1 **13.** A composition of claim 1, wherein said composition is a dosage form
2 selected from the group consisting of a lozenge, a chewing gum, a chewable tablet, and a
3 dissolving tablet.
- 1 **14.** A composition of claim 13, wherein said dissolving tablet is selected
2 from the group consisting of a slow-dissolving tablet and a quick-dissolving tablet.
- 1 **15.** A composition of claim 1, wherein said oral mucosa is selected from
2 the group consisting of the sublingual mucosa, the buccal mucosa, and a combination thereof.
- 1 **16.** A composition of claim 1, further comprising a 5-HT antagonist.
- 1 **17.** A composition of claim 1, further comprising a non-steroidal anti-
2 inflammatory drug (NSAID).
- 1 **18.** A composition of claim 1, wherein the average particle size of said 5-
2 HT agonist or a pharmaceutically acceptable salt thereof is less than or equal to the average
3 particle size of said carrier.
- 1 **19.** A composition of claim 1, wherein said 5-HT agonist is sumatriptan
2 and said ternary buffer system comprises sodium carbonate, sodium bicarbonate, and
3 amorphous magnesium oxide.
- 1 **20.** A composition of claim 19, wherein said composition is a lozenge or a
2 dissolving tablet.
- 1 **21.** A composition of claim 20, wherein said composition is administered
2 sublingually.
- 1 **22.** A composition of claim 19, wherein said sodium bicarbonate is
2 dessicant-coated sodium bicarbonate.

1 **23.** A composition of claim 19, wherein the weight percent of amorphous
2 magnesium oxide is greater than the combined weight percent of sodium carbonate and
3 sodium bicarbonate.

1 **24.** A composition of claim 23, wherein said composition comprises from
2 about 2.5 to about 4.5 weight percent sumatriptan; from about 4.0 to about 7.0 weight percent
3 sodium carbonate; from about 8.0 to about 12.0 weight percent dessicant-coated sodium
4 bicarbonate; and from about 20 to about 30 weight percent amorphous magnesium oxide.

1 **25.** A composition of claim 24, wherein composition comprises about 3.5
2 weight percent sumatriptan; about 5.5 weight percent sodium carbonate; about 9.0 weight
3 percent dessicant-coated sodium bicarbonate; and about 25 weight percent amorphous
4 magnesium oxide.

1 **26.** A composition for delivery of a 5-HT agonist across the oral mucosa,
2 said composition comprising:

3 (a) a 5-HT agonist or a pharmaceutically acceptable salt thereof;

4 (b) a carrier; and

5 (c) a ternary buffer system comprising a carbonate salt, a bicarbonate salt, and a
6 citrate, phosphate, or borate salt,

7 wherein said ternary buffer system raises the pH of saliva to a pH greater than about 9.9
8 irrespective of the starting pH of saliva.

1 **27.** A composition of claim 26, wherein said ternary buffer system raises
2 the pH of saliva to a pH of from about 9.9 to about 11 irrespective of the starting pH of
3 saliva.

1 **28.** A composition of claim 26, wherein said 5-HT agonist is selected from
2 the group consisting of sumatriptan, naratriptan, rizatriptan, eletriptan, almotriptan,
3 zolmitriptan, frovatriptan, and combinations thereof.

1 **29.** A composition of claim 26, wherein said carbonate salt is selected
2 from the group consisting of sodium carbonate and potassium carbonate.

1 **30.** A composition of claim 26, wherein said bicarbonate salt is selected
2 from the group consisting of sodium bicarbonate and potassium bicarbonate.

1 **31.** A composition of claim 26, wherein said citrate salt is selected from
2 the group consisting of sodium citrate, potassium citrate, calcium citrate, magnesium citrate,
3 and ammonium citrate.

1 **32.** A composition of claim 26, wherein said phosphate salt is selected
2 from the group consisting of monobasic sodium phosphate, dibasic sodium phosphate,
3 monobasic potassium phosphate, dibasic potassium phosphate, monobasic calcium
4 phosphate, dibasic calcium phosphate, monobasic magnesium phosphate, dibasic magnesium
5 phosphate, monobasic ammonium phosphate, and dibasic ammonium phosphate.

1 **33.** A composition of claim 26, wherein said borate salt is selected from
2 the group consisting of sodium borate, potassium borate, calcium borate, magnesium borate,
3 and ammonium borate.

1 **34.** A composition of claim 26, further comprising a metal oxide.

1 **35.** A composition of claim 26, wherein said carrier is selected from the
2 group consisting of a binder, a gum base, and combinations thereof.

1 **36.** A composition of claim 26, wherein said composition is a dosage form
2 selected from the group consisting of a lozenge, a chewing gum, a chewable tablet, and a
3 dissolving tablet.

1 **37.** A composition of claim 36, wherein said dissolving tablet is selected
2 from the group consisting of a slow-dissolving tablet and a quick-dissolving tablet.

1 **38.** A composition of claim 26, wherein said oral mucosa is selected from
2 the group consisting of the sublingual mucosa, the buccal mucosa, and a combination thereof.

1 **39.** A composition of claim 26, wherein the average particle size of said 5-
2 HT agonist or a pharmaceutically acceptable salt thereof is less than or equal to the average
3 particle size of said carrier.

1 **40.** A composition of claim 26, wherein said 5-HT agonist is sumatriptan
2 and said ternary buffer system comprises sodium carbonate, sodium bicarbonate, and a
3 citrate, phosphate, or borate salt.

1 41. A composition of claim 40, wherein said composition is a lozenge or a
2 dissolving tablet.

1 42. A composition of claim 41, wherein said composition is administered
2 sublingually.

1 43. A composition for delivery of a 5-HT agonist across the oral mucosa,
2 said composition comprising:
3 (a) a 5-HT agonist or a pharmaceutically acceptable salt thereof;
4 (b) a carrier; and
5 (c) a buffer system comprising a carbonate salt or a bicarbonate salt and two or more
6 buffering agents selected from the group consisting of a metal oxide, a citrate salt,
7 a phosphate salt, and a borate salt,
8 wherein said buffer system raises the pH of saliva to a pH greater than about 9.9 irrespective
9 of the starting pH of saliva.

1 44. A composition of claim 43, wherein said ternary buffer system raises
2 the pH of saliva to a pH of from about 9.9 to about 11 irrespective of the starting pH of
3 saliva.

1 45. A composition of claim 43, wherein said 5-HT agonist is selected from
2 the group consisting of sumatriptan, naratriptan, rizatriptan, eletriptan, almotriptan,
3 zolmitriptan, frovatriptan, and combinations thereof.

1 46. A composition of claim 43, wherein said carbonate salt is selected
2 from the group consisting of sodium carbonate and potassium carbonate.

1 47. A composition of claim 43, wherein said bicarbonate salt is selected
2 from the group consisting of sodium bicarbonate and potassium bicarbonate.

1 48. A composition of claim 43, wherein said carrier is selected from the
2 group consisting of a binder, a gum base, and combinations thereof.

1 49. A composition of claim 43, wherein said composition is a dosage form
2 selected from the group consisting of a lozenge, a chewing gum, a chewable tablet, and a
3 dissolving tablet.

1 **50.** A composition of claim 49, wherein said dissolving tablet is selected
2 from the group consisting of a slow-dissolving tablet and a quick-dissolving tablet.

1 **51.** A composition of claim 43, wherein said oral mucosa is selected from
2 the group consisting of the sublingual mucosa, the buccal mucosa, and a combination thereof.

1 **52.** A composition of claim 43, wherein the average particle size of said 5-
2 HT agonist or a pharmaceutically acceptable salt thereof is less than or equal to the average
3 particle size of said carrier.

1 **53.** A composition of claim 43, wherein said composition is administered
2 sublingually.

1 **54.** A composition for delivery of a 5-HT agonist across the oral mucosa,
2 said composition comprising:

3 (a) a 5-HT agonist or a pharmaceutically acceptable salt thereof;

4 (b) a carrier; and

5 (c) a binary buffer system comprising a carbonate salt or a bicarbonate salt and a
6 metal oxide,

7 wherein said binary buffer system raises the pH of saliva to a pH greater than about 9.9
8 irrespective of the starting pH of saliva.

1 **55.** A composition of claim 54, wherein said binary buffer system raises
2 the pH of saliva to a pH of from about 9.9 to about 11 irrespective of the starting pH of
3 saliva.

1 **56.** A composition of claim 54, wherein said 5-HT agonist is selected from
2 the group consisting of sumatriptan, naratriptan, rizatriptan, eletriptan, almotriptan,
3 zolmitriptan, frovatriptan, and combinations thereof.

1 **57.** A composition of claim 54, wherein said carbonate salt is selected
2 from the group consisting of sodium carbonate and potassium carbonate.

1 **58.** A composition of claim 54, wherein said bicarbonate salt is selected
2 from the group consisting of sodium bicarbonate and potassium bicarbonate.

1 **59.** A composition of claim 54, wherein said metal oxide is selected from
2 the group consisting of magnesium oxide and aluminum oxide.

1 **60.** A composition of claim 59, wherein said magnesium oxide is
2 amorphous magnesium oxide.

1 **61.** A composition of claim 54, wherein said binary buffer system
2 comprises sodium carbonate and amorphous magnesium oxide.

1 **62.** A composition of claim 54, wherein said binary buffer system
2 comprises sodium bicarbonate and amorphous magnesium oxide.

1 **63.** A composition of claim 54, wherein said carrier is selected from the
2 group consisting of a binder, a gum base, and combinations thereof.

1 **64.** A composition of claim 54, wherein said composition is a dosage form
2 selected from the group consisting of a lozenge, a chewing gum, a chewable tablet, and a
3 dissolving tablet.

1 **65.** A composition of claim 56, wherein said dissolving tablet is selected
2 from the group consisting of a slow-dissolving tablet and a quick-dissolving tablet.

1 **66.** A composition of claim 54, wherein said oral mucosa is selected from
2 the group consisting of the sublingual mucosa, the buccal mucosa, and a combination thereof.

1 **67.** A composition of claim 54, wherein the average particle size of said 5-
2 HT agonist or a pharmaceutically acceptable salt thereof is less than or equal to the average
3 particle size of said carrier.

1 **68.** A composition of claim 54, wherein said 5-HT agonist is sumatriptan
2 and said binary buffer system comprises sodium carbonate or sodium bicarbonate and
3 amorphous magnesium oxide.

1 **69.** A composition of claim 68, wherein said composition is a lozenge or a
2 dissolving tablet.

1 **70.** A composition of claim 69, wherein said composition is administered
2 sublingually.

1 71. A composition of claim 68, wherein the weight percent of amorphous
2 magnesium oxide is greater than the weight percent of sodium carbonate or sodium
3 bicarbonate.

1 72. A composition for delivery of a 5-HT agonist across the oral mucosa,
2 said composition comprising:

3 (a) a 5-HT agonist or a pharmaceutically acceptable salt thereof;

4 (b) a carrier; and

5 (c) a binary buffer system comprising a carbonate salt or a bicarbonate salt and a
6 -citrate, phosphate, or borate salt,

7 wherein said binary buffer system raises the pH of saliva to a pH greater than about 9.9
8 irrespective of the starting pH of saliva.

1 73. A composition of claim 72, wherein said binary buffer system raises
2 the pH of saliva to a pH of from about 9.9 to about 11 irrespective of the starting pH of
3 saliva.

1 74. A composition of claim 72, wherein said 5-HT agonist is selected from
2 the group consisting of sumatriptan, naratriptan, rizatriptan, eletriptan, almotriptan,
3 zolmitriptan, frovatriptan, and combinations thereof.

1 75. A composition of claim 72, wherein said carbonate salt is selected
2 from the group consisting of sodium carbonate and potassium carbonate.

1 76. A composition of claim 72, wherein said bicarbonate salt is selected
2 from the group consisting of sodium bicarbonate and potassium bicarbonate.

1 77. A composition of claim 72, wherein said carrier is selected from the
2 group consisting of a binder, a gum base, and combinations thereof.

1 78. A composition of claim 72, wherein said composition is a dosage form
2 selected from the group consisting of a lozenge, a chewing gum, a chewable tablet, and a
3 dissolving tablet.

1 79. A composition of claim 78, wherein said dissolving tablet is selected
2 from the group consisting of a slow-dissolving tablet and a quick-dissolving tablet.

1 **80.** A composition of claim 72, wherein said oral mucosa is selected from
2 the group consisting of the sublingual mucosa, the buccal mucosa, and a combination thereof.

1 **81.** A composition of claim 72, wherein the average particle size of said 5-
2 HT agonist or a pharmaceutically acceptable salt thereof is less than or equal to the average
3 particle size of said carrier.

1 **82.** A composition of claim 72, wherein said 5-HT agonist is sumatriptan
2 and said binary buffer system comprises sodium carbonate or sodium bicarbonate and and a
3 citrate, phosphate, or borate salt.

1 **83.** A composition of claim 82, wherein said composition is a lozenge or a
2 dissolving tablet.

1 **84.** A composition of claim 83, wherein said composition is administered
2 sublingually.

1 **85.** A composition for delivery of a 5-HT agonist across the oral mucosa,
2 said composition comprising:

3 (a) a 5-HT agonist or a pharmaceutically acceptable salt thereof;

4 (b) a carrier; and

5 (c) a binary buffer system comprising a metal oxide and a citrate, phosphate, or
6 borate salt,

7 wherein said binary buffer system raises the pH of saliva to a pH greater than about 9.9
8 irrespective of the starting pH of saliva.

1 **86.** A composition of claim 85, wherein said binary buffer system raises
2 the pH of saliva to a pH of from about 9.9 to about 11 irrespective of the starting pH of
3 saliva.

1 **87.** A composition of claim 85, wherein said 5-HT agonist is selected from
2 the group consisting of sumatriptan, naratriptan, rizatriptan, eletriptan, almotriptan,
3 zolmitriptan, frovatriptan, and combinations thereof.

1 **88.** A composition of claim 85, wherein said metal oxide is selected from
2 the group consisting of magnesium oxide and aluminum oxide.

1 **89.** A composition of claim 88, wherein said magnesium oxide is
2 amorphous magnesium oxide.

1 **90.** A composition of claim 85, wherein said carrier is selected from the
2 group consisting of a binder, a gum base, and combinations thereof.

1 **91.** A composition of claim 85, wherein said composition is a dosage form
2 selected from the group consisting of a lozenge, a chewing gum, a chewable tablet, and a
3 dissolving tablet.

1 **92.** A composition of claim 91, wherein said dissolving tablet is selected
2 from the group consisting of a slow-dissolving tablet and a quick-dissolving tablet.

1 **93.** A composition of claim 85, wherein said oral mucosa is selected from
2 the group consisting of the sublingual mucosa, the buccal mucosa, and a combination thereof.

1 **94.** A composition of claim 85, wherein the average particle size of said 5-
2 HT agonist or a pharmaceutically acceptable salt thereof is less than or equal to the average
3 particle size of said carrier.

1 **95.** A composition of claim 85, wherein said 5-HT agonist is sumatriptan
2 and said binary buffer system comprises amorphous magnesium oxide and a citrate,
3 phosphate, or borate salt.

1 **96.** A composition of claim 95, wherein said composition is a lozenge or a
2 dissolving tablet.

1 **97.** A composition of claim 96, wherein said composition is administered
2 sublingually.

1 **98.** A composition for delivery of a 5-HT agonist across the oral mucosa,
2 said composition comprising:

- 3 (a) a 5-HT agonist or a pharmaceutically acceptable salt thereof;
4 (b) a carrier; and
5 (c) a binary buffer system comprising a carbonate salt and a bicarbonate salt,

6 wherein said binary buffer system raises the pH of saliva to a pH greater than
7 about 9.9 irrespective of the starting pH of saliva.

1 **99.** A composition of claim 98, wherein said 5-HT agonist is sumatriptan
2 and said binary buffer system is combined with sumatriptan to form a solution just prior to
3 delivery of sumatriptan to the oral mucosa.

1 **100.** A composition of claim 98, wherein said 5-HT agonist is sumatriptan
2 and said binary buffer system comprises sodium bicarbonate and sodium carbonate wherein
3 the ratio of sodium bicarbonate to sodium carbonate is from about 2:1 to about 5:1 by
4 weight.

1 **101.** A composition of claim 100, said composition delivering a peak
2 plasma concentration within about 1-15 minutes following administration.

1 **102.** A method for treating a migraine in a subject in need thereof, said
2 method comprising:

3 administering to said subject a composition comprising a therapeutically
4 effective amount of sumatriptan or a pharmaceutically acceptable salt thereof, a carrier, and a
5 binary buffer system comprising a carbonate salt and a bicarbonate salt, wherein said binary
6 buffer system raises the pH of saliva to a pH greater than about 9.9 irrespective of the starting
7 pH of saliva.

1 **103.** A method in accordance with claim 102, wherein said composition is a
2 solution composition.

1 **104.** A method in accordance with claim 103, wherein said binary buffer
2 system comprises sodium bicarbonate and sodium carbonate wherein the ratio of sodium
3 bicarbonate to sodium carbonate is from about 2:1 to about 5:1 by weight, and said
4 composition provides a peak plasma concentration within about 1-15 minutes following
5 administration to said subject.

1 **105.** A method for treating a migraine in a subject in need thereof, said
2 method comprising:

3 administering to said subject a composition comprising a therapeutically
4 effective amount of a 5-HT agonist or a pharmaceutically acceptable salt thereof, a carrier,

5 and a ternary buffer system comprising a carbonate salt, a bicarbonate salt, and a metal oxide,
6 wherein said ternary buffer system raises the pH of saliva to a pH greater than about 9.9
7 irrespective of the starting pH of saliva.

1 **106.** A method of claim **105**, wherein said ternary buffer system raises the
2 pH of saliva to a pH of from about 9.9 to about 11 irrespective of the starting pH of saliva.

1 **107.** A method of claim **105**, wherein said composition delivers said 5-HT
2 agonist across the oral mucosa.

1 **108.** A method of claim **107**, wherein said oral mucosa is selected from the
2 group consisting of the sublingual mucosa, the buccal mucosa, and a combination thereof.

1 **109.** A method of claim **105**, wherein said migraine is selected from the
2 group consisting of a migraine without aura and a migraine with aura.

1 **110.** A method of claim **105**, wherein said 5-HT agonist is selected from the
2 group consisting of sumatriptan, naratriptan, rizatriptan, eletriptan, almotriptan, zolmitriptan,
3 frovatriptan, and combinations thereof.

1 **111.** A method of claim **105**, wherein said carbonate salt is selected from
2 the group consisting of sodium carbonate and potassium carbonate.

1 **112.** A method of claim **105**, wherein said bicarbonate salt is selected from
2 the group consisting of sodium bicarbonate and potassium bicarbonate.

1 **113.** A method of claim **105**, wherein said metal oxide is selected from the
2 group consisting of magnesium oxide and aluminum oxide.

1 **114.** A method of claim **113**, wherein said magnesium oxide is amorphous
2 magnesium oxide.

1 **115.** A method of claim **105**, wherein said ternary buffer system comprises
2 sodium carbonate, sodium bicarbonate, and amorphous magnesium oxide.

1 **116.** A method of claim **105**, wherein said carrier is selected from the group
2 consisting of a binder, a gum base, and combinations thereof.

1 **117.** A method of claim **105**, wherein said composition is a dosage form
2 selected from the group consisting of a lozenge, a chewing gum, a chewable tablet, and a
3 dissolving tablet.

1 **118.** A method of claim **117**, wherein said dissolving tablet is selected from
2 the group consisting of a slow-dissolving tablet and a quick-dissolving tablet.

1 **119.** A method of claim **105**, wherein said oral mucosa is selected from the
2 group consisting of the sublingual mucosa, the buccal mucosa, and a combination thereof.

1 **120.** A method of claim **105**, further comprising a 5-HT antagonist.

1 **121.** A method of claim **105**, further comprising a non-steroidal anti-
2 inflammatory drug (NSAID).

1 **122.** A method of claim **105**, wherein the average particle size of said 5-HT
2 agonist or a pharmaceutically acceptable salt thereof is less than or equal to the average
3 particle size of said carrier.

1 **123.** A method of claim **105**, wherein said 5-HT agonist is sumatriptan and
2 said ternary buffer system comprises sodium carbonate, sodium bicarbonate, and amorphous
3 magnesium oxide.

1 **124.** A method of claim **123**, wherein said composition is a lozenge or a
2 dissolving tablet.

1 **125.** A method of claim **124**, wherein said composition is administered
2 sublingually.

1 **126.** A method of claim **123**, wherein the weight percent of amorphous
2 magnesium oxide is greater than the combined weight percent of sodium carbonate and
3 sodium bicarbonate.